Drug Use Criteria for Ocuvite PreserVision
August 2004
Formulary Agent

GENERIC NAME: High-potency Eye Vitamin and Mineral Supplement

TRADE NAME: Ocuvite PreserVision® (OTC)

FORMULATION: Tablet

USES:
- Appropriate Uses:
  - To delay progression to advanced AMD and prevent visual acuity loss in patients at high risk for AMD (ie, Categories 3 and 4)
    - Category 3: Intermediate-stage AMD with no advanced AMD in either eye
    - Category 4: Intermediate-stage AMD in one eye, advanced AMD in the other
  - To delay progression of AMD in patients with advanced non-exudative AMD in both eyes
- Inappropriate Uses:
  - For the prevention or treatment of any eye disease other than AMD (eg, cataracts)
  - In patients with no AMD (Category 1) or with early-stage AMD (Category 2)
  - In patients with advanced AMD in both eyes, except as above (ie, non-exudative AMD)
  - In patients who are concurrently on high-dose vitamin A, C or E, or high-dose zinc or copper
  - In patients with biliary tract obstruction
  - In patients with Wilson's disease
  - In patients who smoke

FORMULARY RESTRICTIONS:
- Formulary agent
- Restricted to ophthalmologists and optometrists
- Restricted to use criteria

DRUG THERAPY SELECTION:
- Efficacy:
  1. Ocuvite PreserVision was studied in a multicenter, randomized, double-blind, placebo-controlled trial (the Age-related Eye Disease Study [AREDS]).
  2. Patients with Category 2, 3, or 4 AMD (n=3640) were randomized to 4 treatment groups: (1) antioxidants (500 mg of vitamin C, 400 IU of vitamin E, and 15 mg of β-carotene daily); (2) zinc (80 mg of zinc as zinc oxide and 2 mg of copper as cupric oxide daily); (3) combination of antioxidants and zinc; (4) placebo.
  2. Patients at high risk for developing advanced AMD (Categories 3 and 4) reduced their risk of developing advanced stages of AMD by about 25% when treated with the combination of antioxidants and zinc (odds ratio = 0.66; 99% CI: 0.47–0.91; p=0.01).
  3. Patients at high risk for developing advanced AMD who were treated with zinc alone or antioxidants alone reduced their risk of developing advanced AMD by 21% (significant) and 17% (not significant), respectively.
  4. The combination of antioxidants and zinc statistically significantly reduced the risk of visual acuity loss in Categories 3 and 4 AMD (odds ratio = 0.73; 99% CI: 0.54–0.99; p=0.008) as compared to placebo. Zinc alone and antioxidants alone showed favorable trends on this measure, but the differences were not statistically significant.
  5. No statistically significant evidence of a benefit in delaying progression from Category 2 to Categories 3 and 4 was shown in any treatment group.
- Safety:
  1. There was an increase in hospitalization for genitourinary symptoms (7.5% vs 4.9%; p=0.01) in patients given zinc formulations.

2. There was an increase in self-reported anemia (13.2% vs 10.2%; p=0.008) in patients who received zinc formulations. No difference in hematocrit was found, however.
3. Yellow skin was reported more often in the antioxidant treatment groups (8.3% vs 6.0%, p=0.008).
4. The CARET Trial (Beta-carotene and Retinol Efficacy Trial) and the ATBC Trial (Alpha-tocopherol Beta-carotene Cancer Prevention Trial) have demonstrated that supplementation with beta-carotene/vitamin A can significantly increase the risk of lung cancer in smokers. The investigators in the AREDS Trial (the Age-related Eye Disease Study) found no statistically significant difference in mortality based on smoking status, however. Nonetheless, they suggested that it might be prudent for smokers to avoid taking supplements containing β-carotene.
5. The ATBC Trial also reported a higher rate of subarachnoid hemorrhage in smokers given alpha-tocopherol; however, this effect should be weighed against an apparent effect in preventing ischemic stroke.

- Cost:

Product	Cost/Order Unit	Cost/Tablet	Cost/Patient/Year
Ocuvite PreserVision	$10.13/bottle of 120	$0.084	$121.56

Note: No comparable, less expensive product is available to date.

- Risks:
  1. Ocuvite PreserVision should not be confused with other OTC vitamin and mineral combinations for the eyes, such as Ocuvite, Ocuvite Extra, and Ocuvite with Lutein.
  2. Many other high potency vitamin and mineral supplements are available on an over-the-counter basis; patients may inadvertently duplicate therapy.

DUPLICATIVE THERAPY:

- Other high-dose vitamin and mineral products (ask about over-the-counter products)
- Based on a review of the total amounts of vitamins and minerals delivered, concomitant therapy with a typical multivitamin with minerals would not generally be expected to result in toxicity. Caution is warranted, however,

DOSING AND ADMINISTRATION:

- Recommended adult dose (initial and chronic): 2 tablets 2 times daily or as directed by physician.
- Take with food to avoid stomach upset.
- May be used with other vitamin supplements following consultation with a physician or pharmacist.

DRUG-DRUG INTERACTIONS:

- Warfarin: increased hypoprothrombinemic effect occurs with high doses of vitamin A or high doses of vitamin E (>400 IU). Vitamin C can reduce the anticoagulant action of warfarin.
- Iron: iron interferes with the absorption of vitamin E. Absorption of iron increases with co-administration of vitamin C.
- Isotretinoin: concurrent use may increase the risk of vitamin A toxicity.
- Vitamin C: acidifies urine resulting in reabsorption of acidic drugs and an increase in the excretion of basic drugs from the renal tubules (unknown clinical relevance).
- Tetracyclines and fluoroquinolones: zinc decreases the absorption of tetracyclines and fluoroquinolones.
- Copper: absorption of copper is decreased by concurrent use of high doses of zinc or vitamin C.

RECOMMENDED PATIENT MONITORING:

- Clinical:
  1. AMD progression
  2. Visual acuity
  3. GI tolerance
  4. GU tolerance
  5. Evidence of drug interactions

7. Intake of other dietary supplements

- Laboratory:
  1. Renal function (see precautions)
  2. CBC (to confirm suspicion of anemia)

OUTCOME MEASURES:

- Therapeutic:
  1. AMD progression/slowing of progression
  2. Loss of visual acuity
  3. Progression to severe AMD in both eyes (consider discontinuing Ocuvite PreserVision, unless patient has non-exudative AMD)
- Safety/Adverse Effects:
  1. Genitourinary symptoms
  2. Stomach upset
  3. Anemia
  4. Yellow skin

PRECAUTIONS:

- In smokers, β-carotene may increase the risk of lung cancer, and vitamin E may increase the risk of intracranial bleeds (particularly in patients with hypertension). Safety in past smokers is unknown. The potential risks/benefits of treatment with Ocuvite PreserVision in a past smoker should be carefully weighed by the physician in conjunction with the patient.
- High-dose nutraceuticals can interfere with the absorption of other nutrients and medications.
- Patients who have chronic diseases such as cancer, heart disease, and diabetes should use this product with caution.
- Metal accumulation may occur in patients with renal impairment.
- Copper should be avoided in patients with biliary tract obstruction or Wilson's disease.
- Concurrent use of other nutritional supplements should be undertaken with caution.
- Self-medication with high doses of vitamins and minerals—such as those in Ocuvite PreserVision—is generally not recommended.
- See potential drug-drug interactions above.

COMPONENTS AND PHARMACOLOGY:

Components	**Amount per Tablet***	**Mechanism of Action (MOA)**
Vitamin A (β-carotene)	7160 IU	Antioxidant; vitamin A has specialized functions in the conjunctiva, retina, and cornea of the eye; vitamin A deficiency results in xerophthalmia (dry eyes) and nyctalopia (night blindness); macular degeneration is linked with a life-long diet low in β-carotene.
Vitamin C (ascorbic acid)	113 mg	Antioxidant; unknown MOA; vitamin C possibly affects the progression of AMD.
Vitamin E (dl-α-tocopheryl acetate)	100 IU	Antioxidant; vitamin E protects cellular membranes from oxidative damage/destruction.
Zinc (in the form of zinc oxide)	17.4 mg (elemental)	High concentration found in the retinal pigment epithelium; development or worsening of AMD may be associated with zinc deficiency and the loss of zinc-dependent coenzymes in the retinal pigment epithelium.
Copper (in the form of cupric oxide)	0.4 mg (elemental)	No known role in eye diseases; copper was added to offset potential zinc-induced copper deficiency anemia.

*Total daily dose is 4 tablets.